Derivation of induced pluripotent stem cells from orangutan skin fibroblasts.

Journal: BMC Res Notes

Publication Year: 2015

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PubMed link: 26475477

Funding Grants: CIRM Stem Cell Biology Training Program

Public Summary:
Orangutans are among the closest living relatives to humans. For the purposes of the biomedical modeling of human disease and functional genomics studies that can lead into insights about the human genome, we derived induced pluripotent stem cells (iPSCs) from frozen skin cells obtained from captive orangutans. We are the first to demonstrate that orangutan skin fibroblasts are capable of being reprogrammed into iPSCs with hallmark molecular signatures and differentiation potential. This provides opportunities for orangutan cell culture models that would otherwise be impossible to develop from living donors due to the invasive nature of the procedures required for obtaining primary cells.

Scientific Abstract:
BACKGROUND: Orangutans are an endangered species whose natural habitats are restricted to the Southeast Asian islands of Borneo and Sumatra. Along with the African great apes, orangutans are among the closest living relatives to humans. For potential species conservation and functional genomics studies, we derived induced pluripotent stem cells (iPSCs) from cryopreserved somatic cells obtained from captive orangutans. RESULTS: Primary skin fibroblasts from two Sumatran orangutans were transduced with retroviral vectors expressing the human OCT4, SOX2, KLF4, and c-MYC factors. Candidate orangutan iPSCs were characterized by global gene expression and DNA copy number analysis. All were consistent with pluripotency and provided no evidence of large genomic insertions or deletions. In addition, orangutan iPSCs were capable of producing cells derived from all three germ layers in vitro through embryoid body differentiation assays and in vivo through teratoma formation in immune-compromised mice. CONCLUSIONS: We demonstrate that orangutan skin fibroblasts are capable of being reprogrammed into iPSCs with hallmark molecular signatures and differentiation potential. We suggest that reprogramming orangutan somatic cells in genome resource banks could provide new opportunities for advancing assisted reproductive technologies relevant for species conservation efforts. Furthermore, orangutan iPSCs could have applications for investigating the phenotypic relevance of genomic changes that occurred in the human, African great ape, and/or orangutan lineages. This provides opportunities for orangutan cell culture models that would otherwise be impossible to develop from living donors due to the invasive nature of the procedures required for obtaining primary cells.